

The Correlation of Irisin Levels and Some Trace Element as a Potential Mark Diagnosis of Gestational Diabetes Mellitus

Majid Jawad AL-Ghazali¹, Hanaa Addai Ali¹, Mohauman Mohammad AL-Rufaie¹, Rawaa AddayAli²

¹ Department of Chemistry, College of Sciences, Kufa University, Kufa, Iraq

² Department of Microbiology, Collage of Veterinary Medicine AL-Qasim, Green University, Kufa, Iraq

Received: 07 Sep. 2018; Accepted: 04 Nov. 2018

Abstract- The objective of this project was investigating and comparing changes of serum irisin, and trace levels of the elements (Zn, Cu, Mg) in pregnant women with gestational diabetes mellitus GDM in addition to wholesome pregnant group, examining the correlation among (Zn, Cu, Mg) levels and irisin insulin impedance in GDM pregnant women. Sixty GDM pregnant women and thirty wholesome pregnant women were examined. The pair groups were matched for age, and maternal serum irisin. Insulin levels and gestational age were calculated by the assay for enzyme-linked immune sorbent kit at gestation at 24-28 weeks. The confederation between clinical and biochemical parameters and maternal serum irisin levels were predestined. Serum levels of glucose, body mass index, insulin, OGTT, HOMA IR, HOMA β , HbA1c, Hb%, irisin, Zn, Cu and Mg were investigated and analyzed for the examined collection as well as control samples. Pregnant women with GDM disease had noteworthy rising fast blood glucose FBG ($P=0.004$), first-hour OGTT glucose ($P=0.001$), second-hour OGTT glucose ($P=0.001$), fasting insulin FI ($P=0.001$) levels, HOMA IR ($P=0.001$), HOMA β ($P=0.001$), HbA1C ($P=0.001$), Hb% ($P=0.017$), as contrasted to healthy women. Levels of irisin serum were significantly minimizing ($P=0.001$) in women, and sequentially more advanced GDM (mean \pm SD=71.65 \pm 8.03) than healthy pregnant controls (mean \pm SD 136.54 \pm 22.56). Analyses among irisin levels of anthropometric and biochemical values in gestational diabetes patients disclosed that none of the scrupulousness values were remediated with serum irisin level. His present outcomes indicate that the levels of serum irisin might be presented as an incoming GDM marker with decreased irisin levels being GDM symptomatic.

© 2019 Tehran University of Medical Sciences. All rights reserved.

Acta Med Iran 2019;57(1):42-50.

Keywords: Gestational diabetes mellitus; Irisin; Trace elements; Glycemic indices

Introduction

GDM Gestational diabetes mellitus is recognized as a high sensitivity of carbohydrate differing seriousness, by initializing confession through gestation GDM propagation which may ambit domain from (1%-14%) of each gestational, basing on the calculated inhabitance, and the diagnostic test was conducted (1). The GDM pathogenesis is multifactorial and it comprises environmental and genetic parameters, but the accurate mechanism stays to be completely illustrated (2). GDM women are of increased danger for perinatal morbidity, and deteriorated glucose disparity. The kind of diabetes 2 occurs after years of pregnancy. This condition is for woman who may or may not have diabetes before. It goes away after delivery. When a woman is personated

with GDM, there is a risk of having it in the future gestational. Women who had this condition during pregnancy are additionally open to improve diabetes mellitus kind 2 (3). Human pregnancy is described by weight gaining as well as an introductory decrease in the sensitiveness of insulin, which is similar to the fetoplacental growth unity. The insulin impedance of maternity in delayed pregnancy is a paramount mechanism to transfer nutritious substances to the foetus to encourage outgrowth (4). Ordinary pregnancy insulin impedance is furthermore reinforced in pregnancy complexities like those outputs in abnormally foetal outgrowth i.e. intrauterine outgrowth constraint (IUGR) and foetal macrosomia. Neoteric compelling directory proposes that these gestation disturbances are connected by future evolution of maternal metabolic syndrome.

Corresponding Author: M. Mohammad AL-Rufaie

Department of Chemistry, College of Sciences, Kufa University, Kufa, Iraq

Tel: +964 780 9086646, Fax: +964 780 9086646, E-mail addresses: muhaimin.alrufaie@uokufa.edu.iq

Insulin impedance plays an essential functional role in the GDM pathogenesis. In spite of comprehensive research, the basic mechanisms of insulin impedance are not completely comprehended (3). Insulin impedance in gestation is traditionally observed to raise placental hormones as well as maternal adiposity with diabetogenic effect (5). Although the subsidiary mechanisms are not completely realized, the basic fulfillments have concentrated on diverse modern prospective moderators of pregnancy insulin impedance reckonings (6). It is the massive member in the person age, skeletal muscle reckonings by the glucose plurality absorbed in the insulin answer and, quantitatively, the generality essential position for the insulin impedance. Though a past contract, skeletal muscle has been furthermore specified as a secretory member and cytokines as other peptides created and excreted with myocytes and are distributed as myokines (7). These myokines play a role as endocrine hormones.

Irisin is a novel myokine (1), adipokine (2) and neurokine (3) including 112 amino acids, with remaining 12 587 kDa as a molecular weight. Proteolytical treatment from the outcome of fibronectin kind III field includes gene with 5 (FNDC5) in response to the peroxisome energetic proliferator stimulated receptor γ (PPAR γ), co-activator-1 α (PGC-1 α), and the hormone of anti-diabetic that adjusts the metabolism of glucose and energy consuming via transformation white to brown sebaceous tissue (8).

Lately, it has been specified as a practice-encouraged hormone excreted by skeletal muscle and has been suggested as a medium that usefully influences the practice of metabolism (9). A potential danger agent for diabetes mellitus type 2 was sedentary lifestyle. Randomized striped experiments have expounded that physical action evolves glucose toleration and decreases type 2 diabetes mellitus risk (10). For this reason, it has been meditated by physical practice that may usefully influences on the energy through metabolism excreted agents from myocytes such as irisin (7). Later research has shown that widespread irisin amounts are considerably dropping in diabetes type 2 patients in comparison to human without diabetes (11).

Studies on mice have shown that FNDC5 which immediately catalyze the transformations of white greasy tissue (WGT) to brown greasy tissue (BAT), is essential to increase overall energy disbursements; consequently, weight loss, evolved glucose toleration and insulin sensitizing (12). For this reason its metabolic characteristics of irisin have lately been shown of many benefits as a possible modern aim for the treatment of

rotundity and its connected disorders. By clinical frames, widespread irisin amounts are ordinarily minimized for patients by rotundity and (DM) diabetes mellitus type 2 (13), signaling that irisin may have a fundamental function in glucose toleration. After that, widespread irisin is recorded to be contradictorily greater in grown-ups by the metabolic syndrome (14) indicating that conditions of irisin impedance or toleration may occur (15). Information concerning irisin in human gestation is infrequent. Irisin harbinger has been obviously shown in human placenta through the pregnancy and its serum grades to be greater through the entire gestation, when contrasted with nongravid women. After examining the mass of body index BMI, maternal irisin degrees were examined by the homeostasis sample of assessment predestined insulin impedance, suggesting that irisin may contribute in the ordinary evolution pregnancies insulin impedance (7).

The target of the study is to realize and contrast the concentrations of serum irisin between control pregnant women and GDM pregnant women. Irisin grades may have a possible modern marker for diagnosis, a way to keep track of pregnancy diabetes mellitus, estimation of the correlations between Cu²⁺, Zn²⁺ and Mg²⁺, and alteration in the concentrations of serum irisin between healthy pregnant women and pregnant women with GDM.

Materials and Methods

The case-control project was conducted at the Pregnant Care Center, in Najaf, Iraq, between June 2017 and March 2018. The morals committee of the foundation confirmed the project, and all participants provided acquainted consent. The study group comprised 60 women diagnosed with GDM and thirty healthy gravid controls with ordinary glucose toleration test (OGTT) results. All participants were recruited at the screening time for the GDM, utilizing a 75 g, 2-h OGTT between 24 and 28 weeks of pregnancies. GDM was embodied while one or more uncommon amounts of plasma glucose (fasting_92 mg/dL, 1h_180 mg/dL, 2 h_153 mg/dL) were acquired utilizing International Association Criteria of International Association for Diabetes. Also, gestation groups were examined.

The GDM and the groups of control were matched for maternal age, pregnancies age and current (BMI) body mass index. Pregnancies age was determined by the last menstrual interval and assured by ultrasonographic test carried out through the first trimester of pregnancy. BMIs were measured during

Correlation of irisin levels and trace element

OGTT screening using the following formula: weight (kg)/height (m²). No patients received medications that interfered with glucose or lipid metabolism before blood sampling. Patients with doubled gestation, pre- present glucose fanaticism, gestation-motivate preeclampsia, hypertension, chronic inflammation or acute additionally energetic smokers were not included. The venous blood sample of overnight fasting was acquired from all entrants to estimate Iris in levels as well as other biochemical values on the OGTT screening day. A total of specimens were stocked at 25° C at minimal 30 minutes to let the coagulated blood , followed by (3000 rpm) for 15 minute centrifugation to disconnect serum. The samples specimens of serum were taken aliquots and stocked at (80 C) and Iris levels were analyzed. The levels of glucose during OGTT were calculated with the hexokinase project utilizing a commercially obtainable kit (Bio Maghreb, Tunisian). The levels of insulin were specified using a glycosylated hemoglobin (HbA1c) and chemiluminescent assay (USA), and commercially available kits and high-performance liquid chromatography (BIOLABO, France). Homeostatic sample estimation of insulin impedance (HOMA-IR) was determined by the following formula: *fasting glucose (mmol/L) fasting insulin (IU/mL)/22.5*. The

concentrations of magnesium, zinc, and copper on serum were calculated by colorimetric approach using Randox kit (Randox, UK).

The statistical analysis was carried out utilizing two statistical software programs; the Graphpad Prism ver.5 and Statistical Package of Social Science (SPSS ver. 21). Uninterrupted variables were represented as standard deviation (SD)±mean. Significant differences were assessed utilizing double t-test as well as independent t-test for variables with equal and unequal frequencies respectively. Bivariate correlations were assessed using standardized Pearson coefficients. The P amounts obtained of little less than 0.05 and 0.01 were considered as statistically and strongly statistically considerable respectively.

Results

The properties of demography of all participants are shown in Table 1. The total study population was 60 gestational diabetes mellitus, and 30 normal pregnant in each group. The mean of maternal ages, and pregnancies ages of the two collections were not considerable (NS) various. In addition, BMI at the sample collection time varied in both collections.

Table 1. The Demographic characteristics of the study population

Variables	GDM	Control	P
Mother's age (Years)	26.33±3.21	26.07±3.58	0.772 NS
BMI (Kg/m ²) at sampling	34.39±2.00	31.04±1.82	0.000**
Gestational age (weeks) at sampling	28.47±0.96	28.07±0.98	0.069NS

BMI: body mass index.

Clinical data comparisons between the two collections are introduced in Table 2. In the OGTT, HOMA-IR, fasting glucose and insulin amounts are ($P=0.001$). Furthermore Hb% ($P=0.017$) were considerably higher, except HOMAβ ($P=0.001$) which was considerably lower in the group of GDM in comparison with control at the GDM screening time. Serum irisin amounts were considerably lower ($P<0.001$) in women thereafter sophisticated GDM (mean±SD=71, 65±8.03) than in controls (mean±SD 136.54±22.56).

As shown in Table 3, serum Zn amounts were considerably minimized in GDM women as compared to ordinary pregnancy ($P=0.001$). However, serum Cu level appeared significantly lower in the healthy pregnant women compared to GDM collection

($P=0.001$). Conversely, serum Mg levels appeared significantly lower in GDM collection compared to control pregnant women ($P=0.001$).

The relations between serum irisin amounts and other variables analyzed separately at the GDM screening time are in Table 4. In the group of GDM, age significance was ($P=0.025$), while no significant engagements were observed between serum irisin amounts or any other biochemical or clinical parameters.

Discussion

BMI quantities and irisin amounts were observed in women free of diabetes. However, the similar project likewise observed no connection between irisin represented by BMI and myocytes, fasting blood

glucose (FBG), and fasting insulin in diabetic patients. The correlations with positive values between BMI and

widespread irisin amounts in human free of diabetes were observed in the studies of (16,17).

Table 2. Clinical characteristics of healthy pregnant controls and women diagnosed with GDM

Parameters	GDM Mean±SD	Control Mean±SD	P
Glucose(mg/dl)	115.35±11.82	99.00±15.37	0.000**
OGTT(mg/dl) 1h	182.04±4.23	133.23±5.22	0.000**
OGTT(mg/dl) 2h	149.38±8.19	103.11±2.15	0.000**
Insulin (µlu/ml)	15.32±2.70	8.63±1.20	0.000**
HOMA IR	2.51±0.22	1.97±0.21	0.000**
HOMO β	103.00±23.86	84.70±6.92	0.000**
HbA1C%	5.08±0.23	4.47±0.19	0.000**
Hb %	11.70±0.77	11.27±0.81	0.017*
Irisin (ng/ml)	71.65±8.03	136.54±22.56	0.000**

OGTT: oral glucose tolerance test, HbA1c: Glycated hemoglobin A_{1c}, Hb: Hemoglobin

Table 3. Correlations between irisin levels with other biochemical parameters in control subjects and in women diagnosed with GDM

Parameters	R	P
Glucose(mg/dl)	-0.240 NS	0.065
OGTT(mg/dl)1hr.	-0.232 NS	0.074
Insulin(µlu/ml)	-0.038NS	0.774
OMMA IR	-0.154 NS	0.241
HOMMA β	0.044 NS	0.740
HbA1C(%)	-0.077 NS	0.558
Hb(%)	0.038 NS	0.773

Table 4. Comparisons of trace Elements in patients with gestational diabetes mellitus and control group

Parameters	Groups	Mean±SD	P
Cu(µg/dl)	GDM	109.00±14.62	0.001**
	Control	85.43±5.06	
Zn(µg/dl)	GDM	79.27±6.87	0.001**
	Control	101.30±7.20	
Mg(mg/dl)	GDM	1.99±0.07	0.001**
	Control	2.35±0.07	

Several projects have discovered the correlations of positive values between low-density lipoprotein cholesterol and irisin (18). uncovered the correlations of positive values between HDL levels and irisin in chronic renal failure patients. Compared to our oucomes (19) did not discover any correlation between lipid profile and irisin.

The correlations of negative values between HOMA-IR scores and irisin levels were shown. In our project, although likewise we obtained the correlations of negative values between HOMA-IR scores and irisin levels, they were not statistically significant.

Table 5. The relevance of irisin with concentrations of trace element parameters in the patients group

Parameter	R	P
Cu(µg/dl)	-0.164	0.031*
Zn(µg/dl)	0.151	0.735NS
Mg(mg/dl)	0.376	0.033*

Cu:copper, Zn:zinc, Mg: magnesium, **=significant differences at 1%.

It was elucidated that serum irisin of pregnant women was positively conjugated with insulin, fasting glucose and HOMA-IR. Ebert *et al.*, (20) likewise discovered a positive connection between insulin circulating and irisin; however, only in the GDM subgroup. Otherwise, Yuksel *et al.*, (21), stated that irisin level of serum was negatively conected with HOMA-IR. In the current study, the concentration of irisin in the healthy women conected with OGTT and DI120, utilized as the measurements of the sensitivity of insulin additionally beta cell reparations, and negatively with insulin level and HOMA-IR at 120 minutes for the OGTT. A positive connection of insulin sensitivity with circulating irisin.

Identically, studies on the concentrations of blood irisin in GDM women elucidated conflicting resuts, with some of them showing decreasing irisin levels, suggesting that irisin may have an essential function in glucose intolerance and others elucidating no variations

Correlation of irisin levels and trace element

in the irisin levels of maternal between GDM women and control pregnant women (22).

Furthermore stated in tubby Chinese adults, serum irisin was considerably negatively conected HbA1c and fasting insulin .On another hand, Liu *et al.*, discover that widespread irisin was considerably positively conected with fasting blood glucose (23). futhermore stated that widesread irisin was conected with positively with fasting glucose as well as homeostasis sample appreciation of insulin impedance (HOMA-IR). Everyone was established that irisin amounts were positively conected with fasting as well as 2 h post-load insulin amounts, additionally were negatively conected with insulin- catalyzed glucose conductance as well as insulin riddance (24). did not discover a combination between blood glucose levels as well as serum irisin, but instituted that irisin of serum was positively conected with insulin amounts.

Elucidated that serum irisin in pregnant women was positively conected with HOMA-IR as well as fasting glucose, insulin. (25) instituted a positive connection between insulin and widesread irisin, but ultimately in the GDM subgroup. In dissimilarity (26).

Stated that level of serum irisin was negatively conected with HOMA-IR. In the sitting project, the outcomes connecting insulin impedance-conected disorders to irisin are dialectically. Numerous of researchs discover lower widesread circulating irisin amounts in type 2 DM patients.

Likely, studies on the concentrations of blood irisin in GDM women elucidated dialectical outcomes , with sundry of them appearing lower irisin amounts, submitting that irisin may take part an essential function in the intolerance of glucose and with another elucidating no variations in maternal irisin amonuts between GDM women as well as control pregnant women.

Several article groups discover that decreased irisin amounts in long-term recently obtained as well as indefinite type 2 DM contrasted with controls with non-diabetic. Decreasing irisin amounts have been free conected with macrovascular complexities in type 2 DM In disparity Stated no variation in irisin amounts between type 2 diabetic as well as non-diabetic persons. Moreover, irisin amounts were either negatively or positively conected with glucose homeostasis-linked values in type 2 DM patients It appears that there should be some other parameters conected with the irisin levels of blood. Initial (27) had discover a reverse conection between plasma irisin as well as the HbA1c. The appearing variation in HbA1c amounts between

normal control pregnant women as well as GDM patients is proportionate with preceding studies aforementioned. But variations of the average of the HbA1c of everyone group among researchs were shown. In addendum, there were variations of severance amount of HbA1c between our project and previous former researchs. We supposed that these contradictions are perform by ethnical variations which have been obtained previously.

Relations between the levels of serum irisin and trace element parameters at the patients group sgnificant in Table 5. Negative correlations were obtained between Cu ($r=-0.164$, $P=0.031$) but Non Significant positive correlations were obtained between Zn ($r=0.151$, $P=0.735$).while obviously positive connections were obtained between Mg ($r=0.376$, $P=0.033$) Significant.

The deficiency connections of between rope cord plasma zinc as well as the doses of copper not permit to affirm that in every one person case, at submission, a zinc increasing concentration may minimize the copper existent concentration ,as could be anticipated from the recognized antibiosis between the copper and zinc elements (28). Notwithstanding, the evolutionarily directions in placental transmit of copper as well as zinc were obviously. Apparent the outcomes offered feel bad here for the two metals in the mother's plasma as well as rope blood plasma of term toddlers are identical to those stated stated previously (29). Furthermore it was obsreved as the management of magnesium ion concentration to the mother for the tocolysis penetrates the placenta additionally basically equiponderates with foetal, indicating a promulgation incident. The passing neonate hyper magnesemia, subsequently maternal magnesium, remediation is good authenticated. A management of magnesium through action shows to have an extra outcome in connection to the zinc placental transmit. The infromation acquired appear a connection between rope plasma zinc as well as magnesium. It is not obvious whether an impulse in zinc promulgation conecate to magnesium management, or another velum incident, are implicated in this approach. The recognized gestation hypercupremia (30). Obsreves to be a lot of remarkable in those women who transported precocious. Synchronous, maternal ceruloplasmin resorts to diminish as GA increasing. This is proportionate with the decline inclination of the copper plasma from mother to bantling, which is additional remarkable in 24-28-week GA newborns than in the more overripe bantling. The outcomes we gained appear that the concentration of rope plasma ceruloplasmin is much little than the particular maternal

amounts. A preceding study in the previous researchs furthermore appeared a sundry -fold variation between rope blood plasma as well as maternalcopper (31).

However although, the project utilized highly than three contract ago as well as the ultimate amounts educe questions concerning thoroughness. The parsimonious of copper conveyance of to the foetus is proportionate with its disability to composition highly qunatities of ceruloplasmin, or, as alternative, a physiologically outcome of the largely zinc inflow into the foetus chamber, which prevents copper transmission by an increasing of placental metallothionein. This prospect is corroborated by the discovering of minimum copper concentrations in the fetuses liver of rats fed with largely zinc nourishment than in ordinary fed controls (32) The ceruloplasmin test for ultizing this project is based on the so-called

(GDM) Gestational diabetes mellitus is the metabolic disorder through gestation leading to acute and chronic complications in both mother and newborn. Thus, GDM patients have an increasing danger of co-morbidities through pregnancies, e.g. pregnancy-induced hypertension, preeclampsia, as well as houlder dystocia with d hindered submission. Moreover, inveterate complexities might happened after transmission contained cardiovascular disease as well as (T2DM) type 2 diabetes mellitus (33).

For this reason, premature prosopopoeia and suitable GDM remediation of is beneficial in decreasing the inverse maternal as well as foetal consequences additionaaly in conserving mothers as well as pickaninny from long-term. complexities consequently, preceding researchs have attempted to locate the oracular amount of maternal or placental biofactors before the GDM evlution, a swell as these specified in a lot of biological approach containing insulin resistance, oxidative stress, additionally inflammation, carbohydrate metabolism (27). To the good of present knowing, this outcome are the initial to utilize a state-control project to caluclate the serum irisin of GDM patients as well as healthy controls in Iraqi population. Moreover in the current lead to this analyses to appreciate the widespread irisin between healthy controls pregnant as well as GDM patients. Harmonious with these findings, this study assured that GDM pregnant have lower widespread irisin. Involved in the disturbances of the maternal metabolic conected with foetal abnormal evolution. Gestation is connected fundamental with maternal metabolism changes, which supply adequate energy as well as nutrients to the foetus (34). In this situation, mothers improve a status of

insulin impedance thought mid pregnancy that advances the third trimester leading to reduced consumption of glucose by maternal tissues and increased during gluconeogenesis (13). whilst, in an essential ratio of pregnancies, the resistant of insulin- status is extremely excessed product to inverse the condition of maternal metabolic as well as foetal outgrowth aberrations (3).

Irisin is a modern adipokine as well as myokine which encouraged an increasing in overall energy of body disbursements meliorative glucose tolerance as well as insulin sensibility in empirical animals. In the current project showed that the levels of serum irisin were largely lower in the GDM patients than in the healthy control pregnant women, the current outcomes are agreement with the findings of .who futher more communicated a lower in widespread irisin in GDM women that lead to increase in serum irisin with largely amount in pregnant women, but this increasing was largely lowering in objects with GDM (35). The irisin increased largely concentration from colostrum to transmission additionally overripe milk, the plasma irisin as well excessed in lactating GDM women as well as without GDM as comparsion with non-lactating women (26). In GDM, there is enhanced ability of glucose to cross the placenta, with resultant fetal hyperglycaemia, hyperinsulinaemia and macrosomia. This may lead to a variety of fetal pathologies postpartum and pregnancy associated morbidity, such as preeclampsia (36) and susceptibility to development of GD in subsequent pregnancies. Up to 90% of GDM afflicted women develop type 2 diabetes (37). GDM may therefore, serve to unmask women who are predisposed and destined to improve diabetes type 2 last in life (38). Give no variation in widespread irisin between gravid women without as well as with GDM, although however after the birth with 4 years irisin levels were geartly extremely in patients with preceding gestational diabetes mellitus than in the women with normal glucose tolerance reciprocally (39). additional other studies (25).

Showed lower serum irisin in GDM lactating women as comparing with healthy contoal lactating women. No greatly variations in serum irisin between obese, non-obese as well as GDM objects at interval were lately recorded (40), additional studies uncovered that after the regulating for lipids, BMI, glucose as well as irisin levels were geartly lower in pregnant women with non-obese state as comparsion with the obese as well as GDM groups. Our results showed that the irisin levels were markedly minimize than healthy control pregnant, disagreement with other studies that may propose a

Correlation of irisin levels and trace element

reparations for a physiologic increasing in insulin impedance or an activating influence of high levels of the estrogens (10) or its probably extra excretion by the placenta, though the placental tissue influence to widespread irisin shows Unintentionally (41). The researchers introduced that these returns may reason irisin impedance evolving with each other with insulin impedance.

The connotation of irisin impedance resistance with compensative hyper irisinemia was too suggested (42). Who appeared that great irisin levels were conjected with an increasing of the metabolic syndrome danger additionally cardiovascular diseases? However, a connection between insulin impedance as well as irisin in especially through pregnancy, appears as yet unclear. (43). Confirmed that in serum irisin of pregnant women was positively conjected with HOMA-IR, insulin as well as fasting blood glucose (23). Introduced that the level of serum irisin was negatively conjected with HOMA-IR. In persons with diverse obesity degree. Further, we shown that in the entire group of serum irisin concentration of pregnant women conjected negatively with the glucose level at 120 min for the OGTT, that is proportionate with the outcomes (44). Who discover that the glucose of 2 h plasma was a separate negative foreteller for the concentration of irisin in the patients with recently -diagnosed diabetes type 2. Everyone these contradictions may outcome from variations in clinical properties of the objects intended as well as diverse gauges; As though, the potential effect of weight earning or BMI through gestational week as well as pregnancy at specimen taken appears controversial since a positive conjection between body mass index as well as the level of irisin at the final weeks in third gestation trimester. Were studied by various researchers. In the current study, no conjections between BMI as well as circulating irisin were shown. Furthermore, dialectical outcomes, i.e. largely the concentration of irisin in pregnant than in women with non-pregnant (45) or no largely variations through as well as after pregnancy have been establish in various researchs.

In the present study suggest that this element also contributes at some level to the pathogenesis of GDM and pregnancy in diabetes. This is consistent with the role of this metal as an organizer of carbohydrate metabolism in pregnancy (46). The diabetes influence in pregnancy may arise through two related mechanisms, namely, the direct effect of trace elements and oxidative stress on immune regulation (47). A significant lowering in Zn concentration was appeared in the diet-treated

diabetic group relative to healthy pregnancy which supports the hypothesis that Zn and Cu may perform a function in the mechanisms regulating the immune response (48). Another study found that deficiency of Mg⁺⁺ is associated with immunosuppression in athletes, suggesting that Mg⁺⁺ has a role in immune regulation (49).

did not discover a relation between the levels of magnesium, zinc as well as copper in serum with the gestational hypertension, for this reason, they suggested that these metals might not clinically take part in the gestational hypertension pathogenesis (50). The average of serum amounts of copper, magnesium as well as zinc between the two groups were largely various. For realizing, the function of the electrolytes in serum in GDM highly is project indispensable. The outcomes of the current project appeared that these metals did take an outstanding function in the GDM pathogenesis.

The patients with maternal serum irisin amounts with GDM are largely minimizing likened as matched with healthy control pregnant, while, The present outcomes give that serum irisin amounts might presented as a modern of GDM marker, with minimized amounts of irisin being GDM symptomatic, and revealed that these trace elements Cu, Zn, Mg did play a conspicuous function in the GDM pathogenesis. The essential issues of the combinations between future danger of the metabolic syndrome in mother as well as maternal insulin resistance during pregnancy, necessity to be furthermore classified in future possible projects.

References

1. Dawonauth L, Rademacher L, L'Omelette AD, Jankee S, Yan MY, Jeeawoody RB, et al. Urinary inositol phosphoglycan-P type: near patient test to detect preeclampsia prior to clinical onset of the disease. A study on 416 pregnant Mauritian women. *J Reprod Immunol* 2014;101:148-52.
2. Diaz SO, Pinto J, Graça G, Duarte IF, Barros AS, Galhano E, et al. Metabolic biomarkers of prenatal disorders: an exploratory NMR metabolomics study of second trimester maternal urine and blood plasma. *J Proteome Res* 2011;10:3732-42.
3. Newman J. *To Siri, With Love: A mother, her autistic son, and the kindness of a machine*. Hachette UK, 2017.
4. Stoeckel LE, Arvanitakis Z, Gandy S, Small D, Kahn CR, Pascual-Leone A, et al. Complex mechanisms linking neurocognitive dysfunction to insulin resistance and other metabolic dysfunction. Version 2. *F1000Res*.2016.

5. Koski KG, Burns DH, inventors; McGill University, assignee. Method and apparatus for analyzing amniotic fluid. United States patent US 2012;8:165.
6. Perfetti C. Reading ability: Lexical quality to comprehension. *Sci Stud Read* 2007;11:357-83.
7. Nederveen JP, Joannis S, Snijders T, Parise G. The influence and delivery of cytokines and their mediating effect on muscle satellite cells. *Curr Stem Cell Rep* 2017;3:192-201.
8. Kuipers F, Bloks VW, Groen AK. Beyond intestinal soap—bile acids in metabolic control. *Nat Rev Endocrinol* 2014;10:488.
9. Vij K. Textbook of Forensic Medicine & Toxicology: Principles & Practice-e-book. Elsevier Health Sciences, 2014.
10. Norman RA, Paul SP, eds. *The Last Natural Man: Where Have We Been and Where Are We Going?* Springer, 2017.
11. Preethi DM, Jayanthi VE. Ocular disease diagnosis based on LBP and gabor filter. *Int J Sci Eng Res* 2014;5:297-304.
12. DeBrabander J, Shay JW, Wang W, Nijhawan D, Theodoropoulos P, inventors; University of Texas System, assignee. Targeting emopamil binding protein (ebp) with small molecules that induce an abnormal feedback response by lowering endogenous cholesterol biosynthesis. United States Patent Application US 2016;15:667.
13. Epstein EB. *The Experience of Recovery from Food Addiction*. Michigan: Michigan School of Professional Psychology, 2014.
14. Hackett GI. *Sexual health and wellbeing. Diabetes in Old Age*, 2017.
15. Wahlqvist ML, Krawetz SA, Rizzo NS, Dominguez-Bello MG, Szymanski LM, Barkin S, et al. Early-life influences on obesity: from preconception to adolescence. *Ann N Y Acad Sci* 2015;1347:1-28.
16. Hofmann T, Elbelt U, Stengel A. Irisin as a muscle-derived hormone stimulating thermogenesis—a critical update. *Peptides* 2014;54:89-100.
17. Bakker L, Sleddering MA, Schoones JW, Meinders AE, Jazet I. Pathogenesis of type 2 diabetes in South Asians. *Eur J Endocrinol* 2013;169:R99-114.
18. de la Iglesia R, Lopez-Legarrea P, Crujeiras AB, Pardo M, Casanueva FF, Zulet MA, Martinez JA. Plasma irisin depletion under energy restriction is associated with improvements in lipid profile in metabolic syndrome patients. *Clin Endocrinol* 2014;81:306-11.
19. Iiuber O. Complex problem solving as multistage decision making. *Complex problem solving: The Eur Perspective* 2014;4:151.
20. Galhardo MS. *Integrated Analysis of Transcript-Level Regulation of Human Adipogenesis and Cell Type-Selective Disease Association of High Regulatory Load Genes* [Dissertation]. Luxembourg: University of Luxembourg, 2015.
21. Karras SN, Koufakis T, Fakhoury H, Kotsa K. Deconvoluting the Biological Roles of vitamin D-Binding Protein During Pregnancy: A Both Clinical and Theoretical Challenge. *Front Endocrinol* 2018;9:259.
22. Crume TL, Shapiro AL, Brinton JT, Glueck DH, Martinez M, Kohn M, et al. Maternal fuels and metabolic measures during pregnancy and neonatal body composition: the healthy start study. *J Clin Endocrinol Metab* 2015;100:1672-80.
23. Lam SK. *The health of the elderly in Hong Kong*. Hong Kong University Press, 1997.
24. Nadeem M, Li J, Wang M, Shah L, Lu S, Wang X, et al. *Unraveling Field Crops Sensitivity to Heat Stress: Mechanisms, Approaches, and Future Prospects*. *Agronomy* 2018;8:128.
25. Ebert T, Stepan H, Schrey S, Kralisch S, Hindricks J, Hopf L, et al. Serum levels of irisin in gestational diabetes mellitus during pregnancy and after delivery. *Cytokine* 2014;65:153-8.
26. Lal M. *Women's psychosomatic health promotion and the biopsychosociocultural nexus. Clinical Psychosomatic Obstetrics and Gynaecology: A Patient-centred Biopsychosocial Practice*. Oxford Med Online, 2017.
27. Blei F. Literature watch. Emerging roles of the Angiopoietin-Tie and the ephrin-Eph systems as regulators of cell trafficking. *Lymphatic Res Biol* 2018;16:397-417.
28. Bhutta ZA, Das JK, Rizvi A, Gaffey MF, Walker N, Horton S, et al. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? *Lancet* 2013;382:452-77.
29. Premalatha M, Tabassum-Abbasi, Abbasi T, Abbasi SA. The generation, impact, and management of e-waste: State of the art. *Crit Rev Environ Sci Technol* 2014;44:1577-678.
30. Goulding R. *Handbook of dental pharmacology and therapeutics*. Elsevier, 2013.
31. Mather LE. *Stereopharmacological research in anaesthesiology*, 2015.
32. Heaney RP. Nutrition and risk for osteoporosis. In: Marcus R, Dempster D, Cauley J, Feldman D, eds. *Osteoporosis*. 4th ed. Waltham, MA: Academic Press, 2013:645-81.
33. Hu FB, Malik VS. Sugar-sweetened beverages and risk of obesity and type 2 diabetes: epidemiologic evidence. *Physiol Behav* 2010;100:47-54.

Correlation of irisin levels and trace element

34. Leddy MA, Power ML, Schulkin J. The impact of maternal obesity on maternal and fetal health. *Rev Obstet Gynecol* 2008;1:170.
35. Agudelo LZ, Femenía T, Orhan F, Porsmyr-Palmertz M, Gojny M, et al. Martínez-Redondo V. Skeletal muscle PGC-1 α 1 modulates kynurenine metabolism and mediates resilience to stress-induced depression. *Cell* 2014;159:33-45.
36. Spong CY, Mercer BM, D'Alton M, Kilpatrick S, Blackwell S, Saade G. Timing of indicated late-preterm and early-term birth. *Obstet Gynecol* 2011;118:323.
37. Mahmoud F, Abul H, Dashti A, Al-Jassar W, Omu A. Trace elements and cell-mediated immunity in gestational and pre-gestational diabetes mellitus at third trimester of pregnancy. *Acta Medica Academica* 2012;41:175-85.
38. Carolan M, Gill GK, Steele C. Women's experiences of factors that facilitate or inhibit gestational diabetes self-management. *BMC Pregnancy Childbirth* 2012;12:99.
39. Buchanan TA, Xiang A, Kjos SL, Watanabe R. What is gestational diabetes? *Diabetes Care* 2007;30:S105-11.
40. Dubuc-Messier G, Caro SP, Perrier C, van Oers K, Réale D, Charmantier A. Gene flow does not prevent personality and morphological differentiation between two blue tit populations. *J Evol Biol* 2018;31:1127-37.
41. Houser CM. Neonatal Topics. In *Pediatric Development and Neonatology*. New York, NY: Springer, 2014:35-141.
42. Pajari J. Correlation of endogenous secretory receptor for advanced glycation end product (esRAGE) with metabolic health related biomarkers of skeletal muscle. (Accessed March 2018, 12, at <https://jyx.jyu.fi/bitstream/handle/123456789/52090/URN-NBN-fi-jyu-201612014862.pdf?sequence=4>).
43. Rahimi R, Karimi J, Khodadadi I, Tayebinia H, Kheiripour N, Hashemnia M, et al. Silymarin ameliorates expression of urotensin II (U-II) and its receptor (UTR) and attenuates toxic oxidative stress in the heart of rats with type 2 diabetes. *Biomed Pharmacother* 2018;101:244-50.
44. O'Brien MD, Rhoads RP, Sanders SR, Duff GC, Baumgard LH. Metabolic adaptations to heat stress in growing cattle. *Domest Anim Endocrinol* 2010;38:86-94.
45. Wawrusiewicz-Kurylonek N, Telejko B, Kuzmicki M, Sobota A, Lipinska D, Pliszka J, et al. Increased maternal and cord blood betatrophin in gestational diabetes. *PLoS One* 2015;10:e0131171.
46. Jenkins A, Lengyel I, Rutter GA, Lowe N, Shai I, Tirosh A, et al. Obesity, Diabetes and Zinc: A Workshop Promoting Knowledge and Collaboration Between the UK and Israel, November 28-30, 2016–Israel. *J Trace Elem Med Biol*. 2018 Sep;49:79-85.
47. Drutel A, Archambeaud F, Caron P. Selenium and the thyroid gland: more good news for clinicians. *Clin Endocrinol* 2013;78:155-64.
48. Prasad AS. Discovery of Human Zinc Deficiency: Its Impact on Human Health and Disease. *Adv Nutr* 2013;4:176-90.
49. Laires MJ, Monteiro C. Exercise, magnesium and immune function. *Magnes Res* 2008;21:92-6.
50. Jain S, Sharma P, Kulshreshtha S, Mohan G, Singh S. The role of calcium, magnesium, and zinc in pre-eclampsia. *Biol Trace Elem Res* 2010;133:162-70.